

PRO 140



Drug Class: Entry and Fusion Inhibitors

Drug Description

PRO 140 is a humanized monoclonal antibody designed to block the ability of HIV to enter and infect cells. [1]

HIV/AIDS-Related Uses

PRO 140 is an investigational entry inhibitor being studied for the treatment of HIV infection. The drug is in Phase Ib studies and has been granted fast-track status by the FDA.[2]

Pharmacology

PRO 140 inhibits entry of HIV into cells by preventing virus-cell binding at a distinct site on the CCR5 coreceptor without interfering with the normal function of CCR5.[3] The CCR5 receptor is found on certain human inflammatory cells; HIV uses this receptor as a portal to enter and infect healthy cells. PRO 140 exhibits dose-dependent binding to CCR5-expressing cells, significantly coating and protecting such cells for up to 60 days.[4] The synergistic effect seen when combining PRO 140 and other investigational CCR5 inhibitors suggests that PRO 140 may represent a distinct subclass of CCR5 inhibitors.[5]

A Phase I, randomized, double-blind, placebo-controlled study was conducted to examine the safety, pharmacokinetics, and pharmacodynamics of single-dose PRO 140 in 20 healthy males. Participants received intravenous PRO 140 doses of 0.1, 0.5, 2, and 5 mg/kg in sequential, dose-rising cohorts of 5 (4 active, 1 placebo) each and were evaluated for 60 days post-treatment. Serum concentrations of PRO 140 increased proportionally to dose; the serum half-life was approximately 2 weeks. Cellular CCR5 receptors remained coated with PRO 140 for greater than 60 days at the 5 mg/kg dose. No anti-PRO 140 antibodies were observed in preliminary bioanalytical testing.[6] [7]

PRO 140 exhibited potent, broad-spectrum activity in laboratory studies of more than 40 genetically diverse HIV strains. The strains failed to develop resistance to PRO 140, even after 40 weeks of

continued exposure in vitro.[8]

Adverse Events/Toxicity

PRO 140 was generally well tolerated in a Phase I study conducted in healthy volunteers. No infusion-related toxicities, drug-related adverse effects, or electrocardiogram changes occurred with single doses ranging from 0.1 to 5 mg/kg.[9]

Drug and Food Interactions

PRO 140 exhibits potent and reproducible synergy in vitro with investigational small molecule CCR5 antagonists, such as SCH-D, and with the entry inhibitor enfuvirtide.[10]

Clinical Trials

For information on clinical trials that involve PRO 140, visit the ClinicalTrials.gov web site at <http://www.clinicaltrials.gov>. In the Search box, enter: PRO 140 AND HIV Infections.

Dosing Information

Mode of Delivery: Intravenous.[11]

Dosage Form: Intravenous infusions of 0.1, 0.5, 2, and 5 mg/kg doses of PRO 140 have been administered in clinical trials.[12] [13]

Chemistry

CAS Number: 674782-26-4[14]

Molecular formula: Unspecified[15]

Other Names

PRO-140[16]

Further Reading

Castagna A, Biswas P, Beretta A, Lazzarin A. The appealing story of HIV entry inhibitors : from discovery of biological mechanisms to drug

PRO 140



Further Reading (cont.)

development. *Drugs*. 2005;65(7):879-904.

Initial results for PRO 140. *AIDS Patient Care STDS*. 2005 Nov;19(11):780.

Rusert P, Kuster H, Joos B, Misselwitz B, Gujer C, Leemann C, Fischer M, Stiegler G, Katinger H, Olson WC, Weber R, Aceto L, Gunthard HF, Trkola A. Virus isolates during acute and chronic human immunodeficiency virus type 1 infection show distinct patterns of sensitivity to entry inhibitors. *J Virol*. 2005 Jul;79(13):8454-69.

Trials begin for PRO 140. *AIDS Patient Care STDS*. 2004 Nov;18(11):678-9.

Manufacturer Information

PRO 140

Progenics Pharmaceuticals, Inc.
777 Old Saw Mill Road
Tarrytown, NY 10591

For More Information

Contact your doctor or an AIDSinfo Health Information Specialist:

- Via Phone: 1-800-448-0440 Monday - Friday, 12:00 p.m. (Noon) - 5:00 p.m. ET
- Via Live Help: http://aidsinfo.nih.gov/live_help Monday - Friday, 12:00 p.m. (Noon) - 4:00 p.m. ET

References

1. Progenics Pharmaceuticals - Products: HIV Therapeutics-Blocking HIV cellular entry: PRO 140. Available at: http://www.progenics.com/Products/HIV/HIV_PRO140.htm. Accessed 06/20/06.
2. Progenics Pharmaceuticals - Investors: Press Release-Progenics Pharmaceuticals' HIV Drug, PRO 140, Receives FDA Fast-Track Designation [press release], February 22, 2006. Available at: <http://ir.progenics.com/releasedetail.cfm?ReleaseID=192542>. Accessed 06/20/06.
3. Progenics Pharmaceuticals - Products: HIV Therapeutics-Blocking HIV cellular entry: PRO 140. Available at: http://www.progenics.com/Products/HIV/HIV_PRO140.htm. Accessed 06/20/06.
4. Progenics Pharmaceuticals - Investors: Press Release-Progenics Pharmaceuticals' HIV Drug, PRO 140, Receives FDA Fast-Track Designation [press release], February 22, 2006. Available at: <http://ir.progenics.com/releasedetail.cfm?ReleaseID=192542>. Accessed 06/20/06.
5. Int Conf AIDS - 3rd, 2005. Abstract TuOa0206.

PRO 140



6. Conf Retroviruses Opportunistic Infect - 13th, 2006. Abstract 515.

7. Progenics Pharmaceuticals - Investors: Press Release-Progenics Reports Positive Results from Phase 1 Clinical Trial of PRO 140, a Novel Monoclonal Antibody That Blocks HIV Entry [press release], September 9, 2005. Available at: <http://files.shareholder.com/downloads/PGNX/33545428x0x35550/812310b8-774c-4959-8da5-e367079fee27/35550.pdf>. Accessed 06/20/06.

8. Progenics Pharmaceuticals - Investors: Press Release-Progenics Reports Positive Results from Phase 1 Clinical Trial of PRO 140, a Novel Monoclonal Antibody That Blocks HIV Entry [press release], September 9, 2005. Available at: <http://files.shareholder.com/downloads/PGNX/33545428x0x35550/812310b8-774c-4959-8da5-e367079fee27/35550.pdf>. Accessed 06/20/06.

9. Conf Retroviruses Opportunistic Infect - 13th, 2006. Abstract 515.

10. International AIDS Conf - 3rd, 2005. Abstract TuOa0206.

11. International AIDS Conf - 3rd, 2005. Abstract WePe6.2C04.

12. International AIDS Conf - 3rd, 2005. Abstract WePe6.2C04.

13. Conf Retroviruses Opportunistic Infect - 13th, 2006. Abstract 515.

14. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 06/20/06.

15. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 06/20/06.

16. ChemIDplus - Available at: <http://chem.sis.nlm.nih.gov/chemidplus/chemidlite.jsp>. Accessed 06/20/06.